REMARKS

The Office Action of March 4, 2011, has been carefully studied. Claims 1, 2, 6, 7, 9 and 14-17 currently appear in this application. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration and formal allowance of the claims.

Interview Summary

Applicant's attorney wishes to thank Examiner Ricci for the courtesies extended during the telephone interview of April 28, 2011. During that interview, Examiner Ricci confirmed that, the formula on page 4 of the Office Action of March 4, 2011 is considered to be analogous to the claimed compounds and therefore renders the claimed compounds obvious.

Election/Restriction

It is noted that claims 15-17 have been withdrawn as drawn to a nonelected invention.

Applicant respectfully requests rejoinder of claims 15-17, as they are drawn to methods of using the compounds claimed in claim 1.

Claim Amendments

Claim 1 has been amended to correct an inadvertent typographical error in omitting "is" between R^2 and selected.

Claim 1 has also been amended to revise the definition of Q in Formula 2 to require that the purinyl group be substituted with W in the fixed position.

Claim Objections

Claim 1 is objected to because it recites, "R^2 selected from".

Claim 1 has been amended in accordance with the Examiner's helpful suggestions.

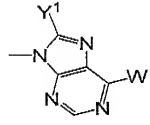
Claim 14 has been amended to delete redundant language.

Art Rejections

Claims 1, 2, 6, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al., WO 2003/029209.

This rejection is respectfully traversed.

Claim 1 has been amended to restrict the definition of Q to :



That is, the compounds claimed in claim 1 have a substituent W in at a specific position on the purinyl group.

Compound 29 of Adams cannot have a substituent group at this position because of the presence of a nitrogen atom at that position in the ring, which cannot accept additional substitution.

However, the carbon atom in this position in the claimed compounds can accept a substituent W. Therefore, one skilled in the art would have no reason to add a substituent W to the Adams compound.

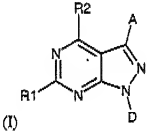
Adams describes a large number of pyrazolo-pyrimidine derivatives and compound 29 is only one of many such compounds. The Federal Circuit has provided criteria for determining the obviousness of chemical compounds, in particular, attention is directed to *Takeda Chemical Industries, Ltd. V. Alphapharm Pty., Ltd.* 492 F.3e 1350 (Fed. Cir. 2007), in which the court said:

> "That test for prima facie obviousness for chemical compounds is consistent with the legal principles enunciated in KSR. While the KSR Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" is an obviousness determination. KSR, 127 S. Ct at 1731. Moreover the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the Graham analysis." Id. As long as the test is not applied as a "rigid an mandatory" formula, that test can provide "helpful insight" to an obviousness inquiry. Id. Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have lead a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound" (at 1356-1357).

In *Daichi Sankyo Co., Ltd. V. Matrix Laboratories*, 619 F.3d 1346 (Fed. Cir. 2010), the Court said,

> Proof of obviousness based on structural similarity requires clear and convincing evidence e that a medicinal chemist of ordinary skill would have been motivated to select and then to modify a prior art compound (e.g., a lead compound) to arrive at a claimed compound with a reasonable expectation that the new compound would have similar or improved properties compared with the old. (at 1352).

In the present case, the Examiner asserts that the herein claimed compounds are obvious by selecting compound 29 of Adams as the example. However, Adams discloses a series of compounds represented by the general formula



(I)

The general formula of Adams covers a huge number of compounds, any of which may be selected for further investigation by one skilled in the art. However, there is no reason to select the compound of Example 29. in this regard, the Examiner fails to provide an adequate reason to support the obviousness rejection.

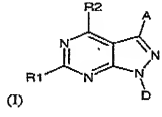
The compounds claimed herein are heteroarylphenylurea derivatives. The compounds of Adams are pyrazolo-pyrimidine derivatives. It is not understood how one skilled in the art would

modify a pyrazolo-pyrimidine derivative to obtain a heteroarylphenylurea derivative with any expectation of obtaining a useful compound.

In guidelines provided to examiners after *KSR v. Teleflex*, the "USPTO has cited *Eisai Co. v. Dr. Reddy's Labs, Ltd.*, 533 F.3d 1533 (Fed. Cir. 2008) as Example 4.11, and provided the following "teaching point":

> A claimed compound would not have been obvious where there was no reason to modify the closest prior art lead compound to obtain the claimed compound and the prior art taught that modifying the lead compound would destroy its advantageous property. Any known compound may serve as a lead compound when there is some reason for starting with that lead compound and modifying it to obtain the claimed compound.

As stated above, the compounds disclosed in Adams have the formula



(I)

The specification of Adams contains the following statement:

> The present invention relates to pyrazolo[3,4-d]-pyrimidine derivatives, compositions and medicaments containing the same, as well processes for the preparation and use of such compounds,

> compositions and medicaments. Such pyrazolo[3,4-d]pyrimidine derivatives are useful in the treatment of diseases associated with inappropriate angiogenesis. (Page 1, lines 5 to 6)
>
> The present inventors have discovered novel pyrazolo-[3,4-d]pyrimidine compounds, which are inhibitors of one or more of TIE-2 kinase activity, VEGFR-2 kinase activity, and VEGFR-3 kinase activity, e.g., one or both TIE-2 kinase and VEGFR-2 kinase activity. Such pyrazolo[3,4-d]-pyrimidine derivatives are useful in the treatment of disorders, mediated by at least one of inappropriate TIE-2kinase, VEGFR-2 kinase, and VGFR-3 activity (which may include cancer and/or disorders characterized by inappropriate angiogenesis; and/or for treating cancer and/or a disease afflicting mammals which si characterized by cellular proliferation in the area of disorders associated with neo-vascularization and/or vascular permeability. (Page 3, lien 28 to page 4, line 8)

From this Ts can readily be understood that the pyrazolo-[3,4-d]pyrimidine moiety of the Adams compounds is indispensible for exhibiting TIE-2 kinase activity, VEGFR-2 kinase activity and VEGFR-3 kinase activity, and is effective for treating disorders mediated by these kinase activities.

On the other hand, the compounds claimed herein do not include a pyrazolo-[3, 4 d]pyrimidine moiety in the structure. Therefore, the compounds claimed herein could not be achieved by modifying compound 29 of Adams without changing its indispensible moiety. However, it is clear that one skilled in the art would not

be motivated to convert the pyrazolo-[3, 4,f]pyrimidine moiety to another structure.

The Examiner has provided no reasoning why one skilled in the art would modify a pyrazolo-[3, 4,f]pyrimidine moiety-containing compound to obtain a heteroarylphenylurea derivative. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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